Remarks

The January 20, 2010 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the January 20, 2010 Official Action. Therefore, the initial due date for response is April 20, 2010.

Claims 1-4, 9, 13, 17-20, 25 and 29 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over U.S. Patent 4,906,457 in view of Japanese patent application 07-010772.

The Examiner has also rejected claims 1-4, 9, 13 17-20, 25, and 29 under 35 U.S.C §103(a) as allegedly unpatentable over Jolles et al. (Br. J. Radiol. (1966) 39:12-18) in view of the '457 patent.

The foregoing rejections constitute all of the grounds set forth in the January 20, 2010 Official Action for refusing the present application.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

In view of the present amendment and the reasons set forth in this response, Applicants respectfully submit that the 35 U.S.C. §103(a) rejections of claims 1-4, 9, 13, 17-20, 25, and 29, as set forth in the January 20, 2010 Official Action, cannot be maintained. These grounds of rejection are, therefore, respectfully traversed.

CLAIMS 1-4, 9, 13, 17-20, 25, AND 29 ARE NOT RENDEREDED OBVIOUS BY THE '457 PATENT IN VIEW OF THE '772 APPLICATION

Claims 1-4, 9, 13, 17-20, 25 and 29 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '457 patent in view of the '772 application. The '457 patent allegedly discloses the topical administration of

soybean trypsin inhibitors for reducing the risk of skin cancer caused by sunlight or other ultraviolet radiation. The '772 application allegedly teach that soybean trypsin inhibitors include Kunitz-type soybean trypsin inhibitors. It is the Examiner's position that it would have been obvious to a skilled artisan to combine the above disclosures to arrive at the instantly claimed invention.

Applicants respectfully disagree with the Examiner's position. Claim 1 of the instant application, from which claims 2-4, 9, and 13 depend, is drawn to methods of reducing the risk of cutaneous tumor development in skin cells that have not yet been damaged by ultraviolet radiation comprising topical application of at least one composition containing a non-denatured soy product in an amount of from about 0.01 to about 99% by weight in a carrier, wherein the non-denatured, soy product comprises a non-denatured, Kunitz-type soybean trypsin inhibitor. Similarly, amended claim 17, from which claims 18-20, 25, and 29 depend, is drawn to methods of reducing the risk of ultraviolet radiation-induced skin cancer in skin cells that have not been damaged by ultraviolet radiation comprising topical application of at least one composition containing a non-denatured, soy product in an amount of from about 0.01 to about 99% by weight in a carrier, wherein said non-denatured, soy product comprises a non-denatured, Kunitz-type soybean trypsin inhibitor.

Kunitz-type soybean trypsin inhibitor is a different inhibitor than the Bowman-Birk protease inhibitor (BBI; see, for example, page 4, bottom paragraph). For example, Gladysheva et al. (Biochemistry (Mosc) (1999) 64(11):1244-9) teach that BBI is capable of binding trypsin, chymotrypsin, and chymotrypsin-like proteases whereas the Kunitz-type soybean trypsin inhibitor is only a trypsin inhibitor. Notably, the Kunitz-type soybean trypsin inhibitor is a more heat labile inhibitor than BBI (see page 4, bottom paragraph). However, the instant application demonstrates that the Kunitz-type trypsin inhibitor is also a more effective inhibitor of

tumor growth than BBI as demonstrated in Table 1; Figures 1 and 2; and Example 1 of U.S. Patent Application No. 10/108,248, from which the instant application depends. The instant application also incorporates the entire disclosure of U.S. Patent Application No. 10/108,248 by reference (see, e.g., page 1, lines 6-10).

In contrast, the '457 patent only teaches the use of "chymotrypsin and trypsin families of protease inhibitors" and only specifically exemplifies the use of the soybean-derived Bowman-Birk protease inhibitor (see paragraph bridging columns 1 and 2). Indeed, the '457 patent states that the "soybean-derived Bowman Birk inhibitor family ... [is an appropriate family] of inhibitors for use in the novel compositions and methods of this invention" (column 2, lines 3-6). Moreover, the only soybean product exemplified by the '457 patent is the Bowman-Birk inhibitor, which inhibits chymotrypsin and trypsin (see Example 2). It is also noteworthy that the other "chymotrypsin and trypsin" family of protease inhibitors listed by the '457 patent is potato inhibitor 1 family (column 2). As with the Bowman Birk inhibitor family, the potato inhibitor 1 family of proteases inhibits chymotrypsin (see, e.g., InterPro Accession No. IPR000864 and U.S. Patent 5,961,980 by Ann Kennedy et al. at column 3, lines 1-17). Therefore, the '457 patent only teaches the anti-cancer properties of chymotrypsin inhibitors and fails to teach or suggest the use of a trypsin specific inhibitor, such as the instantly claimed Kunitz-type soybean trypsin inhibitor.

Additionally, the '457 patent was filed on September 6, 1988. Ten (10) years after the '457 patent was filed, it was still the general understanding in the art that chymotrypsin inhibitors were responsible for the anti-cancer properties of soy. Indeed, Ann Kennedy states that "the ability to inhibit carcinogenesis is associated with the ability to inhibit chymotrypsin" in Kennedy (Amer. J. Clin. Ntr. (1998) 68:1406S-1412S, page 1407S). Moreover, Kennedy states that chymotrypsin inhibitor activity "is present in

soybeans only in BBI" (page 1407S). The '980 patent also states that "protease inhibitors specific for chymotrypsin, but not those that are trypsin-specific, are capable of inhibiting formation of active oxygen species," which are known to contribute to carcinogenicity (at column 3, lines 1-20). Accordingly, even ***ten*** (10) years after the filing of the '457 patent, those of skill in the art believed that the anti-cancer properties of soy were solely attributable to chymotrypsin inhibitors and not trypsin specific inhibitor, such as the instantly claimed Kunitz-type soybean trypsin inhibitor.

The other reference relied on by the Examiner, the '772 application, only discloses that the Kunitz-type soybean trypsin inhibitor suppresses increased inflammatory edema. There is no teaching or suggestion that the Kunitz-type soybean trypsin inhibitor reduces the risk of cutaneous tumor development in skin cells that have not yet been damaged by ultraviolet radiation or reduces the risk of ultraviolet radiation-induced skin cancer in skin cells that have not been damaged by ultraviolet radiation, when administered topically, as instantly claimed.

In addition to all of the above, the instant application provides data that the Kunitz-type soybean trypsin inhibitor and soy product which has not been denatured (e.g., not heat denatured) is unexpectedly superior to the soybean Bowman-Birk protease inhibitor and denatured soy product (see, e.g., Table 1 and Figures 1, 2, and 4 of U.S. Patent Application No. 10/108,248).

In view of the foregoing, it is clear that the instant rejection of claims 1-4, 9, 13, 17-20, 25, and 29 under 35 U.S.C §103(a) is untenable. Withdrawal of the rejection is respectfully requested.

CLAIMS 1-4, 9, 13, 17-20, 25 AND 29 ARE NOT RENDEREDED OBVIOUS BY JOLLES ET AL. IN VIEW OF THE '457 PATENT

The Examiner has also rejected claims 1-4, 9, 13 17-20, 25, and 29 under 35 U.S.C §103(a) as allegedly unpatentable over Jolles et al. (Br. J. Radiol. (1966) 39:12-18) in view of the '457 patent. Jolles et al. allegedly disclose the administration of trypsin inhibitors including soybean trypsin inhibitors to reduce the risk of skin damage due to ultraviolet radiation. The '457 patent allegedly discloses that soybean trypsin inhibitors may be administered topically. It is the Examiner's position that it would have been obvious to a skilled artisan to combine the above disclosures to arrive at the instantly claimed invention.

Applicants respectfully disagree with the Examiner's position and respectfully submit that Jolles et al. has been mischaracterized. Jolles et al. are concerned with "the early tissue changes occurring within minutes after exposure to ionizing radiation" (page 12, left column, first paragraph). Jolles et al. state that "early changes are related to the early phase of the inflammatory reaction in which an increased capillary permeability plays a major role" (page 12, left column, first paragraph). Notably, the experiments performed by Jolles et al. are directed to measure the leakage of plasma from vessels using pontamine sky blue, a blue dye (see Material and Methods generally). Jolles et al. fail to teach or suggest that the capillary leakage is associated with or is even related to the risk of cancer development.

Additionally, Jolles et al. do not administer a singular soybean product to the rabbits in their experiments. Indeed, at page 13, right column, bottom, Jolles et al. teach that their "soya bean trypsin inhibitor (S.B.T.I.)" is actually a "non-specific extract of soya beans" which "inhibits many other proteolytic enzyme systems besides trypsin." In contrast, Jolles et al. note that the ovomucoid trypsin inhibitor (OTI) is specific for trypsin.

Significantly, at page 17, Jolles et al. state that

vascular leakage caused by radiation is greatly reduced or abolished by SBTI, a soy bean extract comprising more than one protease inhibitor. However, OTI, which is a specific trypsin inhibitor, failed to inhibit or reduce vascular leakage despite being administered at concentrations high enough to inhibit any local trypsin (see, e.g., Table 2 and pages 15 and 17). Based on these results, Jolles et al. conclude that "trypsin itself is not the mediator" (page 15, left column, second paragraph). Accordingly, even assuming *arguendo* a link between early capillary leakage and the risk of cancer development, Jolles et al. expressly ***teach away*** from the instant invention by demonstrating that trypsin inhibition had no effect on early capillary leakage.

It is also noteworthy that Jolles et al. administered SBTI intravenously. There is no teaching or suggestion for administering SBTI topically, as instantly claimed.

As explained hereinabove, the '457 patent, the other reference relied upon by the Examiner in the instant rejection, only discloses the use of a chymotrypsin inhibitor. Accordingly, the references cited by the Examiner teach, in combination, that 1) trypsin is ***not*** involved in early vascular changes caused by radiation and 2) chymotrypsin inhibitors such as the Bowman Birk inhibitor can be used to treat skin and reduce the risk of skin cancer associated with exposure to sunlight. It is self-evident that a skilled artisan could not have combined these references to arrive at the instantly claimed methods of using the Kunitz-type soybean trypsin inhibitor to reduce the risk of cutaneous tumor development in skin cells and ultraviolet radiation-induced skin cancer.

In view of all of the foregoing, Applicants submit that the rejection of claims 1-4, 9, 13, 17-20, 25, and 29 under 35 U.S.C §103(a) cannot be reasonable maintained. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendment and remarks, it is respectfully urged that the rejections set forth in the January 20, 2010 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,
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Enclosures: Gladysheva et al., Biochemistry (Mosc) (1999) 64(11):1244-9
InterPro Accession No. IPR000864
Kennedy, A., Amer. J. Clin. Ntr. (1998) 68:1406S-1412S